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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/680,310	10/06/2000	Frank Elischweski	PM268418	9029

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[REDACTED] EXAMINER

LEFFERS JR, GERALD G

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1636

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/680,310	ELISCHWESKI ET AL.
	Examiner	Art Unit
	Gerald G Leffers Jr.	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 27 January 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 29-34 and 36-61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) 56-58 is/are allowed.
- 6) Claim(s) 29-34, 36-55 and 59-61 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. 09/416,756.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 1/27/03 as Paper No. 16, in which claim 35 was cancelled without prejudice. Claims 29-34, 36-61 remain in the instant application and are under consideration.

Further review of the prior art and instant specification indicate that new grounds of rejection are required before any of the pending claims can be allowed to issue. This action is not final because the new grounds of rejection made herein were not necessitated by applicants' amendment of the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-34, 36-55 and 59-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

The rejected claims are drawn towards a method of preparing and improving a pantothenic acid-producing strain of a microorganism comprising amplifying a panE gene in the microorganism and then incubating the microorganism under conditions suitable for the production of the panE gene product, ketopantoate reductase. The specification teaches that the term "amplification" in connection with the claimed invention is intended to mean an increase in

the intracellular activity of one or more enzymes which are coded for by the corresponding DNA by increasing the number of copies of the gene(s), using a potent promoter or a gene which codes for a corresponding enzyme having a high specific activity, and optionally combining the different measures (page 3, lines 3-7). The term “gene” is not explicitly limited by the instant specification to mean just the coding sequence for a given protein, and thus reasonably encompasses those untranslated and/or regulatory elements normally associated with the genomic coding sequence of a given protein (e.g. promoters, untranslated leader sequences, intervening sequences in eukaryotic genes, etc.). The metes and bounds of the words “high specific activity” are not clearly defined in the specification. A reasonably broad interpretation of the phrase is that it encompasses any protein having a specific activity for reduction of ketopantoate. Thus, the rejected claims encompass an enormously broad genus of genes encoding ketopantoate reductase activity from any different microorganism, which may also include untranslated regions normally associated with the gene encoding ketopantoate reductase activity (e.g. intervening sequences in eukaryotic genes). Certain of the claims comprise the same problems directed to additional pantothenic acid pathway genes recited in the claims (e.g. claims 29, 41-43).

Applicants describe the amplification of ketopantoate reductase genes from just two sources, *E. coli* (i.e. a panE gene) and *S. cerevisiae* (the coding sequence encoded by orf YHR063c). No comparison between the nucleic acid sequences obtained from these sources is described, nor are the protein sequences compared. The instant specification does not describe the functional domains within either protein sequence. The specification does not provide the nucleic acid sequences for either of the two exemplified embodiments, although biological

deposits have been made which satisfy the written description requirement for the exemplified embodiments. No description has been provided for the untranslated regions associated with either gene. The specification does not provide a basis for one of skill in the art to envision additional embodiments aside from those exemplified from *E. coli* and *S. cerevisiae*.

The concept of amplifying the *panE* sequence to increase production of pantothenic acid in a microorganism appears to be novel in the art. Apparently, only a single other gene was known in the art to definitely encode ketopantoate reductase activity in a microorganism. Frodyma et al teach the cloning of a gene encoding ketopantoate reductase activity from *S. typhimurium* (i.e. *apbA*) and characterization of the encoded protein's activity in the alternative pyrimidine biosynthetic pathway (Frodyma et al, Journal of Biological Chemistry, March 1998, Vol. 273, No. 10, pages 5572-5576; see the entire reference). Frodyma et al do not explicitly teach the amino acid sequence of the gene encoded by *apbA* nor do they teach the functional domains within the protein. Thus, the prior art does not offset the deficiencies of the instant specification regarding reliably envisioning what additional coding sequences encoding a ketopantoate reductase activity might look like (much less what the non-coding regions of such genes might comprise).

Given the broad genus of potential ketopantoate reductase genes embraced by the rejected claims, and given the lack of any basis for one of skill in the art to reliably predict what additional genes encoding ketopantoate reductase activity might look like, one of skill in the art would not be able to envision a sufficient number of ketopantoate genes to describe the broadly claimed genus of such genes that are to be amplified in the instant claims. Therefore, the skilled

artisan would have reasonably concluded that applicants were not in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejected claims are drawn towards a method of preparing and improving a pantothenic acid-producing microorganism comprising amplifying a panE gene in the microorganism and incubating the microorganism under conditions suitable for the production of the panE gene product. The specification teaches that the term “amplification” in connection with the claimed invention is intended to mean an increase in the intracellular activity of one or more enzymes which are coded for by the corresponding DNA by increasing the number of copies of the gene(s), using a potent promoter or a gene which codes for a **corresponding enzyme** having a high specific activity, and optionally combining the different measures (page 3, lines 3-7) (examiner’s emphasis added).

Claims 29-30, 33-34, 36, 48-50, 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Frodyma et al (Journal of Biological Chemistry, 6 March 1998, Vol. 273, No. 10, pages 5572-5576; see the entire reference). **This is a new rejection.**

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Frodyma et al teach the cloning and expression of the apbA gene from S. typhimurium in E. coli and the purification of its gene product, KPA reductase (i.e. ketopantoate reductase) (e.g. Abstract; Figure 2 and Table 1). At a minimum, the gene taught by Frodyma et al would necessarily be considered the skilled artisan as encoding a *corresponding enzyme* to that encoded by a panE gene because both enzymes comprise the same ketopantoate reductase activity. One of skill in the art could reasonably conclude that the apbA gene characterized by Frodyma et al is a panE gene due to its high ketopantoate reductase specific activity (e.g. Table 1).

Conclusion

Claims 56-58 are allowed. Claims 29-34, 36-55, 59-61 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G. Leffers Jr.
Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
April 7, 2003